

Amendments to the Claims

Claim 1 (previously amended): A combined preparation for simultaneous, separate or sequential use as an ultrasound contrast agent, said preparation comprising:

- i) an injectable aqueous gas dispersion; and
- ii) a separately administrable substance or substances capable of destabilising said dispersed gas so as at least transiently to increase the size thereof.

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Claim 2 (currently amended): A combined preparation as claimed in claim 1 wherein the dispersed gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, ~~an~~-inert gas, a sulphur fluoride, selenium hexafluoride, ~~an~~-optionally halogenated silane, ~~an~~-optionally halogenated low molecular weight hydrocarbon, a ketone, ~~an~~-ester or a mixture of any of the foregoing.

Claim 3 (original): A combined preparation as claimed in claim 2 wherein the dispersed gas comprises sulphur hexafluoride or a perfluorocarbon.

Claim 4 (original): A combined preparation as claimed in claim 3 wherein said perfluorocarbon is perfluoropropane, perfluorobutane or perfluoropentane.

Claim 5 (previously amended): A combined preparation as claimed in claim 1 wherein the dispersed gas is stabilised by an initially coalescence-resisting surface membrane, a

filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.

Claim 6 (original): A combined preparation as claimed in claim 5 wherein said surfactant comprises at least one phospholipid.

Claim 7 (original): A combined preparation as claimed in claim 6 wherein at least 75% of said surfactant comprises phospholipid molecules individually bearing net overall charge.

Claim 8 (original): A combined preparation as claimed in claim 7 wherein said charged phospholipid molecules are selected from phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, phosphatidic acid and cardiolipin molecules.

Claim 10 (previously amended): A combined preparation as claimed in claim 1 wherein said administrable substance further comprises one or more destabilising substances which induce growth of the dispersed gas by flocculation, aggregation, agglomeration, coalescence, fusion or Ostwald ripening.

Claim 11 (currently amended): A combined preparation as claimed in claim 10 comprising one or more destabilising substances selected from the group consisting of inorganic salts, aliphatic alcohols, aliphatic aldehydes, aliphatic ketones, aliphatic esters,

aliphatic ethers, aliphatic amides, aliphatic nitriles, carbohydrates, polyethers, polysaccharides, polyaminoacids, polyvinylpyrrolidone, fatty alcohols, fatty acids, fatty amines, surfactants, steroids, acids, bases and hydrotropes.

Claim 12 (currently amended): A combined preparation as claimed in claim 11 comprising one or more destabilising substances selected from the group consisting of calcium chloride, magnesium chloride, ethanol, isopropanol, ethylene glycol, propylene glycol, glycerol, sorbitol, acetaldehyde, acetone, methyl formate, methyl acetate, propyl formate, ethyl acetate, ethyl methyl ether, methyl propyl ether, di-isopropyl ether, N,N-dimethylformamide, N,N-dimethylacetamide, acetonitrile, glucose, sucrose, polyethylene glycol, polypropylene glycol, polyoxyethylene-polyoxypropylene block copolymers, dextran, starches, polylysine, gelatin, cholesterol, and surface active alkyl carboxylates, alkyl sulphonates, alkyl sulphates, dialkyl sulphosuccinates, alkyl pyridinium salts, alkylammonium salts, alkyl polyethylene glycol ethers, alkyl polyethylene glycol esters and sorbitol fatty acid esters.

Claim 13 (previously amended): A combined preparation as claimed in claim 1 which further includes a vasodilator drug.

Claim 14 (original): A combined preparation as claimed in claim 13 wherein said vasodilator drug is adenosine.

Claim 15 (previously amended): A combined preparation as claimed in claim 1 which further includes a therapeutic drug.

Claim 16 (previously amended): A combined preparation as claimed in claim 1 which further includes contrast-enhancing moieties for an imaging modality other than ultrasound.

Claim 17 (original): A method of generating enhanced images of a human or non-human animal subject which comprises the steps of:

- i) injecting a physiologically acceptable aqueous medium having gas dispersed therein into the vascular system of said subject;
- ii) before, during or after injection of said aqueous medium administering to said subject a substance or substances capable of destabilising said dispersed gas so as at least transiently to increase the size thereof; and
- iii) generating an ultrasound image of at least a part of said subject.

Claim 18 (original): A method as claimed in claim 17 wherein destabilising substance is administered subcutaneously, intramuscularly, intravenously or by inhalation.

Claim 19 (previously amended): A method as claimed in claim 17 wherein a vasodilator drug is coadministered to the subject.

Claim 20 (original): A method as claimed in claim 19 wherein said vasodilator drug is adenosine.

Claims 21-22 (cancelled)

Claim 23 (new): A method of therapeutically treating a human or non-human animal subject which comprises the steps of:

- i) injecting a physiologically acceptable aqueous gas dispersion into the vascular system of said subject;
- ii) before, during or after injection of said aqueous gas dispersion administering to said subject a substance or substances capable of destabilising said dispersed gas;
- iii) growth and retention of said dispersed gas within the tissue microvasculature of the site of interest of said subject and thereby killing cells or blocking the blood flow to the site.

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Claim 24 (new): A method of therapeutically treating a human or non-human animal subject which comprises the steps of:

- i) injecting a physiologically acceptable aqueous gas dispersion into the vascular system of said subject;
- ii) before, during or after injection of said aqueous gas dispersion administering to said subject a substance or substances capable of destabilising said dispersed gas ;
- iii) growth and retention of said dispersed gas within the tissue microvasculature of the site of interest;

- iv) applying ultrasonic irradiation to said site of interest and thereby enhance absorption of ultrasonic energy in hyperthermic therapy.

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